

429 F.3d 1052, 77 U.S.P.Q.2d 1161
(Cite as: 429 F.3d 1052)

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United States Court of Appeals,
Federal Circuit.
INVITROGEN CORPORATION (formerly known
as Life Technologies, Inc.), Plaintiff-Appellant,
v.
CLONTECH LABORATORIES, INC., Defendant-
Cross Appellant.
No. 04-1039, 04-1040.

Nov. 18, 2005.

Background: Patent holder brought infringement action against competitor over patents that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication. The United States District Court for the District of Maryland, Alexander Williams, Jr., J., invalidated claims in patents as anticipated and determined that claims were enabled, satisfied written description requirement, and competitor's products literally infringed certain claims. Parties appealed.

Holdings: The Court of Appeals, Gajarsa, Circuit Judge, held that:

- (1) competitor did not show by clear and convincing evidence that researcher conceived of genetically engineered reverse transcriptase enzyme with no RNase H activity, but having DNA polymerase activity, before critical date;
- (2) fact issue existed as to whether researcher conceived of genetically engineered reverse transcriptase enzyme with no RNase H activity, but having DNA polymerase activity, before critical date;
- (3) declaration by competitor's expert, which merely stated that conception of invention occurred on particular date, combined with extensive attorney argument regarding multiple notebook entries, was inadequate to prove conception;
- (4) patentee fully taught mode of making claimed invention;
- (5) written description requirement had been satisfied;
- (6) complete absence of RNase H activity had to be shown by gel assay; and
- (7) opinion offered by competitor's expert, that differed from opinion offered by patent holder's expert and other scientists regarding interpretation of patent

holder's gel assay evidence, did not create genuine issue of material fact.

Affirmed in part, vacated in part, and remanded.

West Headnotes

[1] Patents 291 ↪ 91(4)

291 Patents

291III Persons Entitled to Patents

291k91 Evidence as to Originality and Priority

291k91(4) k. Weight and Sufficiency in Particular Cases. Most Cited Cases
Competitor did not show by clear and convincing evidence to one of skill in the art that researcher, other than applicant for patent that dealt with molecular biology, conceived of genetically engineered reverse transcriptase enzyme with no RNase H activity, but having DNA polymerase activity, before critical date, where there was no corroborating evidence of researcher's purported belief, and it could not be determined that researcher had reviewed evidence of such discovery and understood its import; research that was being conducted at time was general in nature and it was unknown at time whether it was even possible to make RNase H minus RT with DNA polymerase activity. 35 U.S.C.A. § 102(g)(2).

[2] Patents 291 ↪ 90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(1) k. In General. Most Cited Cases
In a patent case, conception is a legal conclusion premised on various underlying facts. 35 U.S.C.A. § 102(g)(2).

[3] Patents 291 ↪ 90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

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291k90(1) k. In General. Most Cited Cases
In a patent case, conception defines the legally operative moment of invention; it is the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is to be applied in practice. 35 U.S.C.A. § 102(g).

[4] Patents 291 ↪90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(1) k. In General. Most Cited Cases
An idea is sufficiently definite and permanent for conception in the patent context if it provides one skilled in the art with enough guidance to understand the invention, that is, when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. 35 U.S.C.A. § 102(g).

[5] Patents 291 ↪90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(1) k. In General. Most Cited Cases
Conception, in determining priority of invention, requires both the idea of the invention's structure and possession of an operative method of making it. 35 U.S.C.A. § 102(g).

[6] Patents 291 ↪90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(1) k. In General. Most Cited Cases
With regard to a claimed chemical compound, conception requires that the inventor be able to define the compound so as to distinguish it from other materials, and to describe how to obtain it. 35 U.S.C.A. § 102(g).

[7] Patents 291 ↪90(1)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(1) k. In General. Most Cited Cases
An accidental and unappreciated duplication of an invention does not defeat the patent right of one who, though later in time, was the first to recognize that which constitutes the inventive subject matter; thus, the date of conception of a prior inventor's invention is the date the inventor first appreciated the fact of what he made, or, in other words, conception requires that the inventor appreciate that which he has invented. 35 U.S.C.A. § 102(g).

[8] Patents 291 ↪91(3)

291 Patents

291III Persons Entitled to Patents

291k91 Evidence as to Originality and Priority

291k91(3) k. Weight and Sufficiency in General. Most Cited Cases
In a conception inquiry, identifying when, during an emerging recognition that a particular invention includes something new, the inventor's understanding reaches the level needed for appreciation, requires objective corroboration of the inventor's subjective beliefs. 35 U.S.C.A. § 102(g).

[9] Patents 291 ↪91(3)

291 Patents

291III Persons Entitled to Patents

291k91 Evidence as to Originality and Priority

291k91(3) k. Weight and Sufficiency in General. Most Cited Cases
In a conception inquiry, objective evidence is an important part of the appreciation analysis; indeed, because of the danger in post-hoc rationales by an inventor claiming priority, a court requires objective evidence to corroborate an inventor's testimony concerning his understanding of the invention. 35 U.S.C.A. § 102(g).

[10] Patents 291 ↪91(3)

291 Patents

291III Persons Entitled to Patents

291k91 Evidence as to Originality and Priority

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291k91(3) k. Weight and Sufficiency in General. Most Cited Cases

In a conception inquiry, it is not enough that a party adduce evidence that objective test results comport with an inventor's testimony concerning his state of mind; rather, there must also be evidence that the junior party timely interpreted or evaluated the results, and understood them to show the existence the invention. 35 U.S.C.A. § 102(g).

[11] Patents 291 ⚡323.2(3)

291 Patents

291XII Infringement

291XII(C) Suits in Equity

291k323 Final Judgment or Decree

291k323.2 Summary Judgment

291k323.2(3) k. Particular Cases.

Most Cited Cases

Genuine issue of material fact existed as to whether researcher conceived of genetically engineered reverse transcriptase enzyme with no RNase H activity, but having DNA polymerase activity, before critical date, precluding summary judgment on conception issue in infringement lawsuit over patent that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication. 35 U.S.C.A. § 102(g); Fed.Rules Civ.Proc.Rule 56, 28 U.S.C.A.

[12] Patents 291 ⚡91(4)

291 Patents

291III Persons Entitled to Patents

291k91 Evidence as to Originality and Priority

291k91(4) k. Weight and Sufficiency in Particular Cases. Most Cited Cases

Declaration by competitor's expert on summary judgment, which merely stated that conception of invention occurred on particular date, combined with extensive attorney argument regarding multiple notebook entries, was inadequate to prove conception, since expert's statement did not give court any substantive factual guidance and unsubstantiated attorney argument regarding meaning of technical evidence was no substitute for competent, substantiated, expert testimony. 35 U.S.C.A. § 102(g); Fed.Rules Civ.Proc.Rule 56(e), 28 U.S.C.A.

[13] Federal Courts 170B ⚡813

170B Federal Courts

170BVIII Courts of Appeals

170BVIII(K) Scope, Standards, and Extent

170BVIII(K)4 Discretion of Lower Court

170Bk813 k. Allowance of Remedy and Matters of Procedure in General. Most Cited Cases

The denial of a motion for partial summary judgment is reviewed for abuse of discretion. Fed.Rules Civ.Proc.Rule 56, 28 U.S.C.A.

[14] Federal Courts 170B ⚡769

170B Federal Courts

170BVIII Courts of Appeals

170BVIII(K) Scope, Standards, and Extent

170BVIII(K)1 In General

170Bk768 Interlocutory, Collateral and Supplementary Proceedings and Questions

170Bk769 k. On Appeal from Final Judgment. Most Cited Cases

As a general proposition, when a trial court disposes finally of a case, any interlocutory rulings merge with the final judgment; thus, both the order finally disposing of the case and the interlocutory orders are reviewable on appeal.

[15] Patents 291 ⚡99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

Patentee fully taught mode of making claimed invention, for purpose of competitor's claim of lack of enablement of patent that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication, by fully describing operable method for achieving claimed deletion mutation. 35 U.S.C.A. § 112.

[16] Patents 291 ⚡314(5)

291 Patents

291XII Infringement

291XII(C) Suits in Equity

291k314 Hearing

291k314(5) k. Questions of Law or Fact. Most Cited Cases

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In a patent case, enablement is a question of law.

[17] Patents 291 🔑99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

A patent specification must enable those skilled in the art to make and use the full scope of the claimed invention without undue experimentation in order to extract meaningful disclosure of the invention and, by this disclosure, advance the technical arts. 35 U.S.C.A. § 112.

[18] Patents 291 🔑99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

Scope of patent claims must be less than or equal to the scope of enablement; scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation; thus, the enabling disclosure is operational as a limitation on claim validity. 35 U.S.C.A. § 112.

[19] Patents 291 🔑99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

Enablement does not require the inventor to foresee every means of implementing an invention at pains of losing his patent franchise. 35 U.S.C.A. § 112.

[20] Patents 291 🔑99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

Written description requirement had been satisfied, as to patent that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication, where written description recited both DNA and amino acid sequences of representative embodiment

of claimed RT enzyme and specification also disclosed test data that enzyme produced by listed sequence had claimed features of DNA polymerase activity without RNase H activity. 35 U.S.C.A. § 112.

[21] Patents 291 🔑314(5)

291 Patents

291XII Infringement

291XII(C) Suits in Equity

291k314 Hearing

291k314(5) k. Questions of Law or Fact. Most Cited Cases

Unlike conception and enablement, compliance with the written description requirement is a question of fact. 35 U.S.C.A. § 112.

[22] Patents 291 🔑99

291 Patents

291IV Applications and Proceedings Thereon

291k99 k. Description of Invention in Specification. Most Cited Cases

Like the facts underlying conception and enablement, invalidating a patent claim for lack of a written description requires a showing by clear and convincing evidence that the written description requirement has not been satisfied. 35 U.S.C.A. § 112.

[23] Patents 291 🔑90(5)

291 Patents

291III Persons Entitled to Patents

291k90 Original Inventors and Priority Between Inventors

291k90(5) k. Reduction of Invention to Practice in General. Most Cited Cases

In an accidental creation, there is no conception or reduction to practice where there has been no recognition or appreciation of the existence of the new form. 35 U.S.C.A. § 102.

[24] Patents 291 🔑167(1.1)

291 Patents

291IX Construction and Operation of Letters Patent

291IX(B) Limitation of Claims

291k167 Specifications, Drawings, and

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Models

291k167(1.1) k. Specification as Limiting or Enlarging Claims. Most Cited Cases
Complete absence of RNase H activity had to be shown by gel assay, rather than by solubilization assay, as set forth in written description of patent that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication, where specification described gel assay as confirming that plasmid with claimed, modified RT gene, encoded RT that “completely lacked RNase H activity” and primacy otherwise was placed on gel assay results. 35 U.S.C.A. § 112.

[25] Patents 291 ⚡324.5

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k324 Appeal
291k324.5 k. Scope and Extent of Review in General. Most Cited Cases
A district court's partial summary judgment of patent infringement is reviewed de novo. Fed.Rules Civ.Proc.Rule 56, 28 U.S.C.A.

[26] Patents 291 ⚡324.5

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k324 Appeal
291k324.5 k. Scope and Extent of Review in General. Most Cited Cases
A trial court's patent claim construction is a legal issue that is reviewed de novo.

[27] Patents 291 ⚡314(5)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k314 Hearing
291k314(5) k. Questions of Law or Fact. Most Cited Cases
In a patent case, a trial court's comparison of the properly construed claims to the accused products is a factual matter.

[28] Patents 291 ⚡324.5

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k324 Appeal
291k324.5 k. Scope and Extent of Review in General. Most Cited Cases
When reviewing a trial court's partial summary judgment, the Court of Appeals ascertains, as a matter of law, whether the trial court overlooked genuine issues of fact weighing against patent infringement. Fed.Rules Civ.Proc.Rule 56, 28 U.S.C.A.

[29] Patents 291 ⚡161

291 Patents
291IX Construction and Operation of Letters Patent
291IX(A) In General
291k161 k. State of the Art. Most Cited Cases

Patents 291 ⚡167(1)

291 Patents
291IX Construction and Operation of Letters Patent
291IX(B) Limitation of Claims
291k167 Specifications, Drawings, and Models
291k167(1) k. In General. Most Cited Cases

Patents 291 ⚡167(1.2)

291 Patents
291IX Construction and Operation of Letters Patent
291IX(B) Limitation of Claims
291k167 Specifications, Drawings, and Models
291k167(1.2) k. Effect of Drawings. Most Cited Cases

Patents 291 ⚡168(2.1)

291 Patents
291IX Construction and Operation of Letters Patent
291IX(B) Limitation of Claims

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291k168 Proceedings in Patent Office in
General
291k168(2) Rejection and Amendment
of Claims

291k168(2.1) k. In General. Most Cited Cases
Patent claim construction requires the court to determine the meaning of disputed claim terms to one of ordinary skill in the art at the time of the invention; court determines this meaning by examining the claim language, as it relates to the invention set forth in the written description, the drawings, and where relevant, the prosecution history. 35 U.S.C.A. § 112.

[30] Patents 291 ⚡ 168(2.1)

291 Patents
291IX Construction and Operation of Letters Patent

291IX(B) Limitation of Claims
291k168 Proceedings in Patent Office in
General
291k168(2) Rejection and Amendment
of Claims

291k168(2.1) k. In General. Most Cited Cases
A court examines the prosecution history, when pointed out and placed in evidence, to ascertain if a proffered patent claim construction has been disclaimed.

[31] Patents 291 ⚡ 168(2.1)

291 Patents
291IX Construction and Operation of Letters Patent

291IX(B) Limitation of Claims
291k168 Proceedings in Patent Office in
General
291k168(2) Rejection and Amendment
of Claims

291k168(2.1) k. In General. Most Cited Cases
The prosecution of one patent claim term in a parent application will generally not limit different claim language in a continuation application; however, an exception exists where an amendment to a related limitation in the parent application distinguishes prior art and thereby specifically disclaims a later, though differently worded, limitation in the continuation application.

[32] Patents 291 ⚡ 323.2(4)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k323 Final Judgment or Decree
291k323.2 Summary Judgment
291k323.2(4) k. Affidavits or Other Evidence. Most Cited Cases
Opinion offered by competitor's expert, that differed from opinion offered by patent holder's expert and other scientists regarding interpretation of patent holder's gel assay evidence, did not create genuine issue of material fact on summary judgment motion, in infringement lawsuit over patent that disclosed genetically modified enzyme, reverse transcriptase, involved in DNA replication, since opinion offered by competitor's expert was speculative in that he did not cite any basis for it.

[33] Federal Civil Procedure 170A ⚡ 2546

170A Federal Civil Procedure
170AXVII Judgment
170AXVII(C) Summary Judgment
170AXVII(C)3 Proceedings
170Ak2542 Evidence
170Ak2546 k. Weight and Sufficiency. Most Cited Cases
A party does not manufacture more than a merely colorable dispute simply by submitting an expert declaration asserting that something is black when the moving party's expert says it is white; there must be some foundation or basis for the opinion. Fed.Rules Civ.Proc.Rule 56(e), 28 U.S.C.A.

Patents 291 ⚡ 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
5,244,797, 5,688,005. Cited.

Patents 291 ⚡ 328(2)

291 Patents

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291XIII Decisions on the Validity, Construction,
and Infringement of Particular Patents

291k328 Patents Enumerated

291k328(2) k. Original Utility. Most Cited
Cases
6,063,608. Infringed.

*1056Jay I. Alexander, Milbank, Tweed, Hadley & McCloy LLP, of Washington, DC, argued for plaintiff-appellant. With him on the brief were Robert J. Koch and James Pooley. Of counsel on the brief were Kevin R. Casey and Harrie R. Samaras, RatnerPrestia P.C., of Valley Forge, Pennsylvania; and Alan Hammond, Invitrogen Corporation, of Carlsbad, California.

Marc R. Labgold, Patton Boggs LLP, of McLean, Virginia, argued for defendant-cross appellant. With him on the brief *1057 were Michael J. Schaengold, Richard J. Oparil, and Kevin M. Bell.

Before MICHEL, Chief Judge,^{FN*}RADER, and GAJARSA, Circuit Judges.

^{FN*} Paul R. Michel assumed the position of Chief Judge on December 25, 2004.

GAJARSA, Circuit Judge.

Invitrogen appeals from the judgment of the United States District Court for the District of Maryland, invalidating two hundred and twenty-one claims, in three related Invitrogen patents, as anticipated by § 102(g)(2) prior art. *Invitrogen Corp. v. Clontech Labs., Inc.*, Nos. AW-96-4080, AW-00-1879 (D.Md. October 17, 2003) (final judgment) ("*Invitrogen*"). Invitrogen confessed judgment of invalidity based on the district court's underlying ruling that researchers at Columbia University conceived of a similar invention before, and were diligent in reducing it to practice after, Invitrogen's first reduction to practice in 1987. *Invitrogen Corp. v. Clontech Labs., Inc.*, (D.Md. Mar. 18, 2002) (order adopting the Special Master's Report & Recommendation and granting partial summary judgment in favor of Clontech on conception); *Invitrogen Corp. v. Clontech Labs., Inc.*, (D.Md. Jan. 15, 2002) (Special Master's Report and Recommendation on cross summary judgment motions regarding conception). On this appeal, Invitrogen challenges the district court's partial summary judgment dating conception by the Columbia researchers.

On cross-appeal Clontech challenges three underlying partial summary judgments in favor of Invitrogen: (1) that the claims-in-suit are enabled; (2) that the claims-in-suit satisfy the § 112 written description requirement; and (3) that Clontech's products literally infringe claims 3, 4, 12, and 13 of U.S. Patent No. 6,063,608.

We hold that the district court misapplied the law of appreciation when dating conception by the Columbia researchers and ignored genuine issues of fact precluding partial summary judgment in favor of Clontech. Thus, the court vacates the invalidity judgment and the district court's conception ruling and remands for further proceedings. Turning to Clontech's cross-appeal, we affirm the district court's rulings on enablement and written description.

Clontech's remaining cross-appeal challenges the district court's partial summary judgment of literal infringement for Invitrogen. Because we find no error in the district court's claim construction, or its treatment of the facts, we affirm.

I.

A.

Invitrogen owns U.S. Patent No. 5,244,797 ("the '797 patent"), U.S. Patent No. 5,688,005 ("the '005 patent"), and U.S. Patent No. 6,063,608 ("the '608 patent") (the "patents-in-suit"). This appeal involves the '797 patent, claims 1-4; the '005 patent, claims 8-29; and the '608 patent, claims 1-196 (the "claims-in-suit"). All three patents issued from continuations of a common parent application, No. 07/143,396 ("the '396 application"), filed on January 13, 1988, and share a common written description.^{FN1}

^{FN1}.The '797 patent issued on September 14, 1993, from application No. 07/671, 156 ("the '156 application"), filed March 18, 1991. The '156 application was a continuation of the parent '396 application, filed January 13, 1988.

The '005 patent issued September 16, 1997, from application No. 08/614,260 ("the '260 application"). The '260 applica-

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tion, filed on March 12, 1996, traces through a series of continuation applications to a divisional from the '156 application (now issued as the '797 patent).

The '608 patent issued on May 16, 2000, from application No. 08/798,458, filed February 10, 1997, as a continuation of the '260 application (now issued as the '005 patent).

***1058** The patents deal with molecular biology. In particular, the patents disclose a genetically modified enzyme, reverse transcriptase, involved in DNA replication. Reverse transcriptase ("RT") is a naturally occurring enzyme produced by retroviruses, such as the Moloney-Murine Leukemia Virus ("MMLV"). Invitrogen's genetic modifications affect how the modified RT participates in DNA replication.

DNA replication involves a series of discrete steps. The original DNA-a molecule comprised of two strands of nucleotides forming a double helix-is opened to expose single strands. Messenger RNA ("mRNA"), comprising a single strand of nucleotides, forms opposite the exposed DNA strands. The mRNA detaches from the exposed DNA and serves as a template against which a first strand of complementary DNA ("cDNA") forms. This is first strand synthesis. The mRNA detaches from the first cDNA strand, allowing a second, complementary DNA strand to form opposite the first strand, completing the process. This is second strand synthesis. The completed cDNA molecule is a copy of the original DNA transcribed by the mRNA. "Reverse transcription" describes building the cDNA from the mRNA template.

Reverse transcriptase affects at least two steps in this process. First, it facilitates the formation of cDNA opposite the mRNA template, a step called DNA polymerase activity. Second, it degrades the mRNA strand of the mRNA / cDNA hybrid molecule so that the first strand cDNA nucleotides are free to form a second strand and complete the DNA replication. Degrading or destroying the mRNA template is called RNase H activity. Until the mRNA template is removed from the first strand cDNA, the second strand cDNA synthesis cannot occur.

If RNase H activity destroys the mRNA template, as

happens with naturally occurring RT, then it cannot serve as a template for additional cDNA. But if the RNase H activity of RT is inhibited, and the mRNA is detached from the hybrid mRNA / cDNA first strand without being destroyed, then scientists can reuse the mRNA to form additional cDNA. An RT with inhibited RNase H behavior is useful for efficiently cloning DNA.

As described and claimed in the patents, Invitrogen developed mutant RT with DNA polymerase, but no RNase H, activity ("RNase H minus"). More particularly, Invitrogen altered a gene that originally encoded wild or natural RT, resulting in a mutant enzyme with the desired properties. Invitrogen reduced this invention to practice on January 27, 1987.

B.

Invitrogen was not, however, the first to explore the genetics of RT. Beginning in the early 1980s two scientists at Columbia University, Dr. Stephen P. Goff and his post-doctoral researcher, Dr. Naoko Tanese, studied the effects of random mutations in the MMLV gene for RT-an approach called "random mutagenesis." ^{FN2} In 1984, Tanese prepared a panel of roughly 100 mutants. Without sequencing the mutants, ***1059** Goff did not know where the MMLV gene had been altered in each mutation. Two mutant genes created in 1984 were H7 and H8, each encoding enzymes that later proved to lack RNase H activity.

FN2. Goff was the first person to isolate and clone the wild MMLV gene for RT. On May 6, 1985, Goff filed a patent application on a plasmid incorporating that MMLV gene. The application listed Goff, Tanese, and Monica Roth-another researcher in Goff's lab-as inventors. It issued on July 24, 1990, as U.S. Patent No. 4,943,531.

After creating the mutant MMLV genes, Tanese tested the mutant RT they encoded for DNA polymerase activity. Roth tested the mutant RT for a different function called integrase. In late 1984, Tanese also tested the mutant RT for RNase H activity. But the tests using 1984 assay technology yielded inconclusive results. The mutant RT under investigation was produced in *E. coli* bacteria, which naturally produces an enzyme with RNase H activity. The

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RNase H activity of the bacterial enzyme introduced too much background noise to measure, with existing methods, the RNase H behavior of the mutant RT.

The 1984 assay technology could have been used to measure the mutant RT RNase H activity if Goff and Tanese first purified the mutant RT for each mutant MMLV gene—that is, if they had they isolated the mutant RT from the background *E. coli* enzymes. Goff concluded that approach was too time consuming for the large number of mutant MMLV at issue, so he and Tanese developed a new *in situ* assay. That new assay was designed to measure the RNase H activity of the mutant RT without first isolating it from the bacterial enzymes. Not until March 1987, however, did Goff and Tanese complete the new assay and apply it to their panel of mutants.

Nonetheless, in 1986, before finishing the new assay, Goff sequenced various mutant RT genes. Among those he sequenced were H7 and H8.

When Goff and Tanese completed the new *in situ* assay in March 1987, they rapidly determined which parts of the MMLV RT gene affected which enzyme properties. By March 7, 1987, they established that H7 and H8 encoded mutant RT with DNA polymerase activity but no RNase H activity.

Goff and Tanese started publishing their work after March 1987. On January 29, 1988, Goff filed a patent application pertaining to this research. In 1993 the U.S. Patent and Trademark Office (“PTO”) declared an interference between Goff’s application and the ’260 application that eventually issued as Invitrogen’s ’005 patent. (October 18, 1993 notice of interference from PTO). The sole count described a method for producing a genetically modified RT with DNA polymerase but “having substantially no RNase H activity.” Goff’s assignee, Columbia University, defaulted and the PTO ruled in Invitrogen’s favor. As a result, the PTO never reviewed Goff’s research records to determine priority of invention between Goff and Invitrogen. That priority question is now central to this appeal.

C.

This litigation involves using RNase H minus RT to prepare libraries of cloned DNA. The defendant and cross-appellant, Clontech, develops and sells prod-

ucts in the fields of genomics and molecular biology. Clontech has produced cDNA libraries using genetically modified RTs and has sold kits with RNase H minus RT that may be used to prepare cDNA libraries.

On December 31, 1996, Invitrogen, formerly Life Technologies, Inc., accused Clontech of infringing the ’797 patent. It later added the ’005 patent to the suit. Among other contentions, Invitrogen accused Clontech of infringing the ’797 and ’005 patents by selling two products, SuperScript and SuperScript II, other RTs, and cDNA libraries prepared using such enzymes. Clontech responded by asserting*1060 non-infringement, invalidity, and unenforceability.

In 1999, following a bench trial, the district court entered judgment of unenforceability in favor of Clontech on both the ’797 and ’005 patents. The district court ruled that Invitrogen had engaged in inequitable conduct by not citing to the examiner as prior art a presentation by Goff in which he described his work on mutant MMLV RT to a conference at Stanford. On September 21, 2000, this court reversed and remanded. *Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320 (Fed.Cir.2000).

On May 16, 2000, while the appeal on the ’797 and ’005 patents was pending, the ’608 patent issued to Invitrogen. As noted above, the ’608 patent claims priority to the original January 13, 1988, application. On June 22, 2000, Clontech filed a complaint for declaratory judgment of non-infringement, invalidity, and unenforceability of the ’608 patent. Invitrogen counterclaimed that Clontech’s PowerScript RT product infringed the ’608 patent. The district court consolidated this set of claims for trial with the remanded infringement action on the ’797 and ’005 patents.

D.

There followed a series of pre-trial motions regarding Goff’s conception, Invitrogen’s enablement, Invitrogen’s written description, and Clontech’s infringement of the ’608 patent. On June 20, 2001, the district court appointed a Special Master, who reviewed several of those motions.

On January 15, 2002, the Master recommended partial summary judgment in favor of Clontech under §

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102(g)(2), establishing that Goff (1) conceived Invitrogen's invention first, and (2) diligently reduced it to practice. On March 18, 2002, the district court accepted the Master's report and recommendation ("R & R") and granted partial summary judgment in favor of Clontech.^{FN3} Invitrogen now challenges this ruling as to Goff's conception.

FN3. As discussed below, the parties cannot agree on the nature of this ruling.

The district court also entered three other interlocutory orders. First, on May 4, 2001, the court granted partial summary judgment for Invitrogen that the claims-in-suit were enabled. Second, on April 21, 2003, the court granted partial summary judgment in favor of Invitrogen, holding that two Clontech products literally infringed claims 3, 4, 12, and 13 of the '608 patent. Third, on August 11, 2003, the court granted partial summary judgment in favor of Invitrogen, ruling that the claims-in-suit satisfied the written description requirement. On cross-appeal Clontech challenges the following: (1) the ruling that the claims-in-suit were not invalid for lack of enablement; (2) the ruling that the claims-in-suit were not invalid for lacking a written description; and (3) the partial summary judgment of infringement.

* * * * *

Following these rulings and immediately before the scheduled trial, the court adopted this jury instruction on "Anticipation-Prior Invention by Goff":

The Court has already determined that Goff *et al.* invented a mutant [RT] enzyme that did not have RNase H activity. The enzyme was prepared in December 1984, and its reduction to practice was confirmed in March 1987. The Court has also found that Goff was diligent and that he did not abandon, suppress or conceal his invention. Goff's work is available as prior art as of December 1984.

***1061** Faced with this jury instruction, Invitrogen consented to entry of final judgment of invalidity under § 102(g) in view of Goff's work. On October 17, 2003, the district court entered final judgment in both actions (Invitrogen's infringement suit and Clontech's declaratory judgment action), invalidating several claims under § 102(g)(2) in view of Goff: (a) '797 patent, claims 1-4; (b) '005 patent, claims 8-29;

and (c) '608 patent, claims 1-196.

Both parties timely appealed. The court has jurisdiction under 28 U.S.C. § 1295(a)(1).

II.

A.

[1]Section 102(g)(2) provides "[a] person shall be entitled to a patent unless ... before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other." 35 U.S.C. § 102(g)(2) (2000).

Invitrogen and Clontech filed cross summary judgment motions under this section concerning Goff's work at Columbia University. Invitrogen argued that Goff's work could not qualify as prior art to the three patents-in-suit. Clontech contended that Goff's work anticipated the claims-in-suit. In the alternative Clontech sought a ruling on the admissibility, or relevance, of Goff's work as prior art.^{FN4}

FN4. As noted below, Clontech relies on a series of documents—primarily laboratory notebooks kept by Dr. Goff and his assistants throughout the 1984-87 time-frame—as evidencing Dr. Goff's prior invention for § 102(g)(2). The district court entered its invalidity judgment purely on grounds of anticipation; it did not discuss Goff's work as a potential 102(g) / 103 prior art reference.

Although the district court denied both parties' motions, it made several substantive rulings. First, the court determined that on January 27, 1987, Invitrogen actually reduced to practice a genetically altered reverse transcriptase with DNA polymerase activity but no RNase H activity. Second, it held that Goff conceived of a genetically modified reverse transcriptase with no RNase H activity in December 1984 when he produced the H7 and H8 mutants, or at the latest in

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January 1986 when he sequenced the two mutant genes. Third, the court found that Goff actually reduced his invention to practice in March 1987 when he demonstrated the RNase H minus behavior of the H7 and H8 mutants with his new *in situ* assay. Finally, the court found that Dr. Goff was diligent in reducing his invention to practice, and he did not abandon, conceal or suppress it. Notwithstanding these rulings, the court refused to find Dr. Goff's work anticipatory under § 102(g)(2) on grounds that anticipation posed factual questions requiring resolution on a claim by claim basis. Thus, the court appeared to question or leave for the jury's resolution whether its description of the "inventions" by Invitrogen and Goff properly coincided, or whether the claims-in-suit accurately corresponded to the description of Goff's invention.

As a preliminary matter, Clontech contends the district court's order was no more than an evidentiary ruling on the admissibility of Goff's work at trial. This argument has no merit. As demonstrated by the jury instruction on anticipation, the *1062 order established facts and removed legal issues from dispute. The rulings define Invitrogen's invention, date Invitrogen's reduction to practice (if not its conception), date Goff's conception, find diligence, and date his reduction to practice. These are determinations on less than the entire case and less than the whole relief sought by the cross summary judgment motions. The district court expressly premised these rulings on what it viewed as undisputed facts in the record. Thus, the court's determinations comprise an order "specifying the facts that appear without substantial controversy ... and directing such further proceedings in the action as are just." Fed.R.Civ.P. 56(d). Regardless of how the district court labeled its order, it is a partial summary judgment on Goff's conception under § 102(g)(2).

On appeal Invitrogen challenges only the district court's determination that Dr. Goff conceived of a genetically engineered reverse transcriptase with no RNase H before the critical date. As the first step in evaluating Goff's conception under § 102(g)(2), the court must identify two references: (1) the "invention" subject to the priority contest; and (2) the critical date, or the date of Invitrogen's conception. Although the district court appeared to treat its characterization of Dr. Goff's invention and Invitrogen's invention as potentially divergent, Invitrogen effec-

tively concedes two critical points by consenting to judgment of invalidity and limiting its appeal to the date of Goff's conception. First, this eliminates any doubt that Goff's invention, whose conception the district court evaluated, was the same as the Invitrogen invention at issue.^{FN5} Second, this establishes that the court's statement of the invention captures subject matter that anticipates all two hundred twenty-one claims at bar.^{FN6} Furthermore, Invitrogen's failure to challenge the January 27, 1987 critical date effectively establishes its conception, for § 102(g)(2), as simultaneous with its reduction to practice. As Invitrogen does not challenge the court's rulings on diligence, the relevant question on appeal is whether Goff conceived of the invention before January 27, 1987.

^{FN5}. For the same reasons, it frames the dispute in terms of a single Invitrogen invention, rather than multiple inventions spread across the three patents-in-suit.

^{FN6}. The claims-at-bar correspond to the court's statement of the invention. The district court's reasons for deciding priority, but refusing summary judgment, are somewhat unclear.

The court must resolve that question using a properly defined invention. Although the district court described Goff's invention without mentioning DNA polymerase activity, the invention at issue plainly requires this additional limitation. The DNA polymerase activity limitation is manifest in the patent claims, the common written descriptions of the patents-in-suit, and in the purpose of the invention. In short, the court is tasked with dating Dr. Goff's conception of a(1) genetically engineered (2) reverse transcriptase enzyme (3) with no RNase H activity (4) but having DNA polymerase activity.

B.

The court reviews *de novo* a grant of partial summary judgment. Beech Aircraft Corp. v. EDO Corp., 990 F.2d 1237, 1245 (Fed.Cir.1993). Although Invitrogen and Clontech filed cross summary judgment motions, each motion "must be independently assessed on its own merits." California v. United States, 271 F.3d 1377, 1380 (Fed.Cir.2001). Moreover, on summary judgment, the court holds the parties to the same evi-

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dentiary burden they would have faced at trial. ***1063***Apple Computer, Inc. v. Articulate Sys., Inc.*, 234 F.3d 14, 20 (Fed.Cir.2000).

[2] Conception is a legal conclusion premised on various underlying facts. *Singh v. Brake*, 222 F.3d 1362, 1367 (Fed.Cir.2000); *Cooper v. Goldfarb*, 154 F.3d 1321, 1327 (Fed.Cir.1998); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed.Cir.1986). As the partial summary judgment ruling arose in the context of Clontech's motion for summary judgment of invalidity, Clontech was required to identify clear and convincing evidence of the factual underpinnings for Goff's conception. See *Apotex USA, Inc. v. Merck & Co., Inc.*, 254 F.3d 1031, 1036 (Fed.Cir.2001) (requiring the party asserting invalidity to prove by clear and convincing evidence that the invention was not abandoned, suppressed, or concealed under § 102(g)); cf. *Lindemann Maschinenfabrik GMBH v. Am. Hoist and Derrick Co.*, 730 F.2d 1452, 1459 (Fed.Cir.1984).

In sum, the court must affirm the district court's partial summary judgment on conception in favor of Clontech if, in view of the heightened evidentiary burden at trial and drawing all reasonable factual inferences most favorably to Invitrogen, it finds no disputed issue of material fact underlying the conception analysis, and Clontech was entitled to the determination that Goff's conception preceded Invitrogen's. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986).

C.

[3][4][5][6] Conception defines the legally operative moment of invention under § 102(g). It is the “formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.” *Hybritech*, 802 F.2d at 1376. An idea is sufficiently definite and permanent for conception if it provides one skilled in the art with enough guidance to “understand the invention,” that is, “when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue.” *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed.Cir.1994). The inventor must be able to “describe his invention with particularity.” *Id.* This requires both (1) the idea of the invention's structure and (2) possession of an

operative method of making it. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed.Cir.1991). Thus, with regard to a claimed chemical compound, conception requires that the inventor “be able to define” the compound “so as to distinguish it from other materials, and to describe how to obtain it.” *Id.*

[7] This description, and the “definite and permanent idea of the complete and operative invention” for conception, require more than unrecognized accidental creation. “[A]n accidental and unappreciated duplication of an invention does not defeat the patent right of one who, though later in time, was the first to recognize that which constitutes the inventive subject matter.” *Silvestri v. Grant*, 496 F.2d 593, 597 (CCPA 1974). Thus, “[t]he date of conception of a prior inventor's invention is the date the inventor first appreciated the fact of what he made.” *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d 1334, 1341 (Fed.Cir.2001). In other words, conception requires that the inventor appreciate that which he has invented.

D.

The invalidity judgment depends on when Goff appreciated that H7 and H8 were RNase H minus, but retained DNA ***1064** polymerase activity.^{FN7} Invitrogen contends that the district court misread the facts and misapplied the law to award Goff priority of invention. Under a correct application of law, Invitrogen argues, Goff did not conceive of the invention until March 1987, when he perfected his *in situ* assay and established that the H7 and H8 mutants were RNase H minus. Invitrogen contends that until that moment, Goff never recognized that his accidental creations, the H7 and H8 mutants, had the inventive features at issue. Clontech disagrees, and asks the court to affirm the district court's ruling.

^{FN7} The district court did not discuss the DNA polymerase activity of H7 and H8. On appeal, Invitrogen does not separately challenge Goff's timely appreciation of this behavior. Clontech argues that the record demonstrates Goff's recognition of H7 and H8 DNA polymerase activity in 1984. For purposes of this analysis the court assumes that timely appreciation of DNA polymerase activity is not disputed. The parties and the trial court can revisit this issue, as necessary,

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on remand.

Although such conscious problem solving suggests conception comes first, under some conditions conception is delayed until a reduction to practice. *See Burroughs*, 40 F.3d at 1229; *Amgen*, 927 F.2d at 1206; *Alpert v. Slatin*, 49 C.C.P.A. 1343, 305 F.2d 891, 894 (1962).^{FN8} Such delayed conception is often described by the rule against *nunc pro tunc* conception. That is, a reduction to practice at time A necessarily requires the inventor to possess the knowledge about the invention to show a conception. However, the law will not sanction the inference that reduction to practice at time A implies conception at earlier time B.

^{FN8}. “A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete idea as it will be used in practice.” *Burroughs*, 40 F.3d at 1229.

With unrecognized accidental duplication, the invention exists but remains unrecognized. The priority determination requires evidence that the inventor actually first made the invention, and that he understood his creation to have the features that, comprise the inventive subject matter at bar. Thus, the court must identify when, during an emerging recognition that a particular invention includes something new, the inventor's understanding reaches the level needed for appreciation. In the appreciation analysis, the relevant uncertainty relates to the emerging recognition of something new.

[8] That analysis requires objective corroboration of the inventor's subjective beliefs. *Heard v. Burton* illustrates the importance of the inventor's actual knowledge or beliefs. 51 C.C.P.A. 1502, 333 F.2d 239, 243 (1964). In *Heard*, a priority contest arose in an interference proceeding. The “essence of the invention” was “using eta-aluminum, a specific type of hydrated aluminum oxide, as support material for platinum” in a reforming process in which the platinum-alumina combination served as a catalyst. *Id.* at 240. The record showed that the compound could only be identified by its x-ray diffraction pattern. *Id.* at 241 n. 1. The critical date was April 23, 1952,

when Burton filed a patent application on the invention.

Although Heard actually made the novel compound in 1949 and 1950, the record showed that he never recognized it. Only in 1954 did the successor to Heard's work, the Standard Oil Company, confirm by x-ray diffraction analysis that the 1949 compound contained the novel catalyst; only in 1961 did Standard Oil Company—again by *1065 x-ray diffraction—establish that the new catalyst was also present in the 1950 compound. *Id.* at 242. As the court observed, “we consider it fatal to [Heard's] case that not until after the [critical date] did Heard recognize that his ‘ammonia-aged’ catalyst ... ‘contained any different form of alumina at all.’ ” *Id.* at 243. The fact that Heard “relegated the spent catalysts to storage cages” rather than further develop them confirmed the lack of recognition. In short, the inventor-Heard—never suspected what he had created, and the context—a novel compound whose existence is shown by inspecting its x-ray diffraction pattern—required the most specific of objective evidence, which was missing. *Heard* was an easy case.

[9][10] While *Heard* made clear the importance of an inventor's subjective beliefs about his invention, objective evidence is also an important part of the appreciation inquiry. Indeed, because of the danger in post-hoc rationales by an inventor claiming priority, the court requires objective evidence to corroborate an inventor's testimony concerning his understanding of the invention. *See Jolley*, 308 F.3d at 1321 (“Because conception is a mental act, ‘it must be proven by evidence showing what the inventor has disclosed to others and what that disclosure means to one of ordinary skill in the art.’ ”) (quoting *Spero v. Ringold*, 54 C.C.P.A. 1407, 377 F.2d 652, 660 (1967)). Thus, it is not enough that a party adduce evidence that objective test results comport with an inventor's testimony concerning his state of mind. Rather, there must also be evidence that the junior party timely interpreted or evaluated the results, and understood them to show the existence of the invention. *See Langer v. Kaufman*, 59 C.C.P.A. 1261, 465 F.2d 915, 919 (1972).

In *Langer*, the court extended *Heard* to provide that where there is an objective basis for identifying the novel features of an invention, there must be evidence that the inventor timely considered it. The facts

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of the *Langer* interference were essentially identical to those in *Heard*: the invention called for a catalyst using a particular crystalline compound,^{FN9} and as defined in the count the new compound was identified by a characteristic x-ray diffraction pattern. *Id.* at 917-18. But in contrast to *Heard*, Langer photographed x-ray diffraction patterns of the new compound two years *before* the critical date. *Id.* at 919. Reviewing those photos roughly eleven years after the critical date, Langer's co-inventor identified evidence of the new catalyst. *Id.* The problem was that nothing showed, before the critical date, that anyone had either looked at the photos or understood what they meant. Quoting the opinion below, the court observed that there was "no evidence of any contemporaneous interpretation or evaluation of the patterns" by the inventors or anyone working with them. *Id.*

FN9. Specifically, it required the gamma form of crystallized titanium trichloride (TiCl₃) as a co-catalyst component. *Langer*, 465 F.2d at 917.

In *Silvestri v. Grant*, 496 F.2d 593, 597 (CCPA 1974), the court applied these principles to a priority contest in view of a record showing uncertainty in interpreting the test results corroborating the inventor testimony on appreciation. Notwithstanding that uncertainty, the court tested the evidence against the junior party's burden at the interference, and concluded that the record showed appreciation. In short, *Silvestri* requires an objective basis corroborating the inventor's belief to show, consistent with the appropriate burden at trial, that persons skilled in the art at the time of the recognition would have recognized *1066 the existence of the relevant inventive features.^{FN10}

FN10. The invention was "a new form of an otherwise old composition" of ampicillin. *Silvestri*, 496 F.2d at 597. The interfering subject matter, as defined in the count, called for an anhydrous form of ampicillin having improved storage stability and a particular infrared spectrograph. *Id.* at 595-96.

Although *Silvestri* framed the issue as "whether the evidence establishes *beyond a reasonable doubt* that, prior to [the critical date], Silvestri not only actually pre-

pared [the new form of ampicillin], but also appreciated that a new form of ampicillin had been obtained," *id.* at 597 (emphasis added), that high standard does not apply to this case, see *Horwath v. Lee*, 564 F.2d 948, 949 n. 2 (CCPA 1977), and has been replaced by clear and convincing evidence. See *Price v. Symsek*, 988 F.2d 1187, 1194 (Fed.Cir.1993) ("The board erred ... by requiring Price to prove derivation and priority beyond a reasonable doubt rather than by clear and convincing evidence."). The fact that Silvestri could satisfy this high burden, even with ambiguity in the evidence showing the presence of the new compound, demonstrates that appreciation does not require conclusive or unassailable evidence showing existence of a new compound's novel features.

The rule in *Silvestri* has direct application to the genetically engineered RT claimed here. Clontech must show by clear and convincing evidence that Goff formed a timely belief that his H7 and H8 RT were RNase H minus. Once Goff's belief is established, the court must further determine that whatever test results Goff cites, and Clontech relies upon, show by clear and convincing evidence to one of skill in the art at the time that the H7 and H8 mutant RT were RNase H minus.

E.

To the extent the district court may, *inter alia*, have considered appreciation in reaching its conception ruling, its analysis was inadequate. At most, the court seemed to find it undisputed that Goff intended to create RNase H minus RT in 1984 and that by the time he sequenced the H7 and H8 in 1986, Goff completed his conception (and appreciation).

As a matter of law, the court's conclusion is unsustainable. *Langer* and *Silvestri* require some connection between the physical result (the invention) and the belief (by the inventor). Here, the district court never identified corroborating evidence of Goff's purported belief, nor identified how it could determine that Goff had reviewed such evidence and understood its import. There is no evidence that merely sequencing the mutant RT gene could, in 1986, estab-

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lish the corresponding enzyme's properties.

More fundamentally, the record is inconsistent with the district court's notion that Goff set out to create RNase H minus RT, or that he recognized his invention in 1984. It shows, instead, that this action fits squarely within the unrecognized, accidental duplication cases. First, Goff's research was general in nature. The random mutagenesis involved a panel of 100 randomly mutated MMLV RT genes. At his deposition, Goff testified that Tanese's 1984 experiments "[were] focused on understanding what the consequences of those mutations were for the virus." He explained that his "main grant and the main focus of [his] whole lab was to look at the [MMLV] mutants ... and to look at the [effects] of those mutations on the virus." Second, it was unknown at the time whether it was even possible to make an RNase H minus RT with DNA polymerase activity. Not until his March 1987 assay, Goff explained, had anyone shown that RNase H activity involved a separate area of the RT gene from the sequence responsible for DNA polymerase. The publications at the time were conflicting, and it was unclear "whether it would be *1067 possible to express [the two functions] separately because there are many multi function enzymes, but frequently [their] multiple activities are interconnected so intimately, that [it is] very hard to separate them." Finally, asked to identify the time when he "decided" to create an RNase H minus mutant RT, Goff testified that "the belief was that we had them, but I didn't know how to characterize them. *I mean, it wasn't that we wanted one. There was no reason to have one in our minds.*" (emphasis added) Even assuming the district court had assessed an objective basis for appreciation—which it did not—on these facts the partial summary judgment of conception for Clontech is unsustainable.

F.

[11] Although the district court's conception analysis misapplied the law to the facts, this court must examine whether correctly applying the law of appreciation to this record would dictate a different result. See *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 164 (Fed.Cir.1985). As shown below, we cannot affirm the invalidity judgment under a correct application of the law.

1.

Although initially (as shown above) Goff explained that he had no reason to believe that H7 and H8 were RNase H minus, by late 1986 he had formed a suspicion. Asked whether he suspected this behavior in H7 and H8 RT before March 1987, Goff replied:

"Sure. I mean, in the course of all those failed assays, you know, there were hints of things [RNase H] working badly. So that you do develop a feel for what's likely to be the result later But, you know, for publications of quality you've got to convince people. So we needed-it took that long [until March 1987] to get reliable assays." Goff dated his suspicion regarding H8 to "the end of '86 or something because they really weren't working very well for quite a while."

This testimony plainly excludes the district court's dates of Goff's conception, December 1984 or January 1986. But Clontech may still show that Goff's conception took place before January 27, 1987. Put differently, a reasonable fact-finder presented with Goff's testimony could conclude that while Goff appreciated the RNase H minus features of the H7 and H8 RT by March 1987, the evidence preceding the March 1987 test results might also suffice, by clear and convincing evidence, to corroborate Goff's timely suspicions about the H7 and H8 mutants. The question becomes whether, as a matter of law, the trial court ignored a genuine issue of fact that should have been given to a jury.^{FN11}

^{FN11} Relying on Goff's statement concerning the need for academic certainty before he would publish his suspicions, Invitrogen argues that Goff has admitted he did not appreciate the RNase H behavior of the H7 or H8 RT before March 1987. We disagree. The appreciation analysis is objective and depends on the record evidence Clontech adduces or cites in support of its conception argument. The legal test does not depend on subjective factors like an inventor's readiness to publish, art-specific factors like journal publication requirements, career pressure to publish in an academic environment, or grant requirements. Such variable factors are poor proxies for how a person skilled in the relevant art would interpret objective evidence corroborating a purported

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recognition, and we do not believe the law should depend on such malleable parameters. If it did, the law would create a perverse incentive to rush to publication, in order to preserve a conception claim against a potential later priority date. Goff's testimony about wanting more conclusive data, in short, does not prevent a finding of appreciation and conception before the January 27, 1987 critical date.

***1068 2.**

The court thus turns to the objective evidence that might corroborate Goff's suspicion. Clontech urges the court to find Goff's appreciation shown, without any genuine dispute, by a collection of laboratory notebook entries spanning the years 1984 to 1987. On close inspection, however, Clontech's evidence fails to carry its summary judgment burden.

Clontech relies on several notebook entries whose meanings are factually disputed. For example, Clontech argues that entries from December 1984 and May 1985 show Goff was "focused" on testing H7 and H8 as early as December 19, 1984. It further argues that this "focus" demonstrates Goff's understanding that the mutants were RNase H minus. But on inspection neither the December 1984 entry, nor the May 1985 entry, indicates the alleged "focus" on H7 or H8. Each recites a list of several mutants under examination, and Goff's paper concerning this research discusses forty-two mutants.

Other Clontech contentions squarely conflict with inventor testimony interpreting the same underlying notebook entries. For example, Clontech contends that a December 1984 entry provides undisputed evidence that Goff recognized that the H7 and H8 mutants were RNase H minus.^{FN12} But Invitrogen specifically asked Goff, at his deposition, to comment on the entry, and he testified that it was not relevant to the H7 or H8 RT RNase H minus behavior.^{FN13}

^{FN12.} The December 21 and 22 entry reads "clone H7 & H8 (weakly positive on RT assay-12/17/84 Should amplify the signal)."

^{FN13.} Goff responded, "that's cell culture work, so this is not relevant.... [T]here are many distinct issues of function from the

bacterial enzyme."

[12] Overshadowing all of Clontech's arguments are defects in the expert testimony. Clontech nowhere provides the court with expert testimony that properly explains the technical notebook entries advanced in support of its conception arguments. The declaration from Clontech's expert, Joseph O. Falkinham, III, gives the court no substantive factual guidance. Falkinham states, "Based on my review, Goff, et. al. conceived of the claimed invention, RNase H-deficient mutant [MMLV RT] in 1984 It is clear from his testimony and his lab records that he conceived of the invention in 1984." (Falkinham Decl. ¶ 4). Citing various notebook entries, Falkinham asserts "[t]hese representative entries demonstrate Goff's conception, diligence and reduction to practice." (*id.* ¶ 5). But such wholly conclusory assertions on a legal issue cannot carry Clontech's burden on summary judgment. See *Biotec Biologische Naturverpackungen GmbH & Co. KG v. Biocorp, Inc.*, 249 F.3d 1341, 1353 (Fed.Cir.2001).

Although Clontech responds to that evidentiary problem with extensive attorney argument regarding multiple notebook entries, the argument is insufficient. See *id.*; *Am. Airlines, Inc. v. United States*, 204 F.3d 1103, 1112 (Fed.Cir.2000); *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply, Inc.*, 45 F.3d 1550, 1562 (Fed.Cir.1995) ("There must be sufficient substance, other than attorney argument, to show that the issue requires trial."). Unsubstantiated attorney argument regarding the meaning of technical evidence is no substitute for competent, substantiated expert testimony. It does not, and cannot, support Clontech's burden on summary judgment.

***1069** Perhaps Clontech's strongest factual argument concerns January 1987 laboratory notebook entries by Roth, working in Goff's laboratory. The entries record various experiments or "product analyses" or RT assays involving H7, during which Roth added RNase H to various batches under inspection. Essentially, Clontech argues that Roth would not have added RNase H unless the H7 mutant lacked RNase H activity. Thus, Clontech concludes, these entries demonstrate to a person skilled in the art that the H7 RT was RNase H minus. As with its other record citations, however, the problem lies in Clontech's attempt to substitute attorney argument for expert testimony. Nowhere does Clontech point to expert

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testimony explaining what Roth's notebook entries mean. Even if Clontech were correct about their meaning, nothing indicates that they amount to clear and convincing evidence that H7 and H8 were RNase H minus, nor that Goff drew that conclusion from them.

Indeed, the record compels an inference that he did not. At his deposition, Goff testified that Roth's work was directed to testing for integrase activity—an unrelated property of the mutant RT.^{FN14} Insofar as Goff's testimony goes to his subjective recognition of the test results, the issue is similar to that recognized in *Langer*. Goff's testimony demands the inference, on this partial summary judgment, that he did not understand Roth's entries to show that H7 and H8 RT were RNase H minus.

FN14. Invitrogen argues that Goff's testimony forecloses the court from finding appreciation based on these January 1987 notebook entries by Roth. Contrary to Invitrogen's contention, neither its argument nor the record precludes finding timely recognition by Goff. Goff was not responding to a question specifically addressing these notebook entries, and his testimony is too general either to join issue with Clontech's conception argument, or to explain away Roth's entries.

In short, as the factual inferences must be drawn adverse to Clontech, the district court erred in granting partial summary judgment establishing Goff's conception before January 27, 1987.

3.

[13] Finally, Invitrogen argues that the court should reverse the district court's partial summary judgment on conception, rather than merely vacate it. This argument in effect challenges the district court's denial of Invitrogen's motion for partial summary judgment on conception. We review the denial of a motion for partial summary judgment for abuse of discretion. *See Pickholtz v. Rainbow Techs., Inc.*, 284 F.3d 1365, 1371 (Fed.Cir.2002). In view of the foregoing factual discussion, on this record the district court did not abuse its discretion in refusing to grant partial summary judgment for Invitrogen.

III.

[14][15] Clontech's cross-appeal challenges three interlocutory orders by the trial court in favor of Invitrogen. Two were partial summary judgments that the claims-in-suit were not invalid, either for failing enablement or the written description requirements of § 112. The last determined that Clontech infringed four claims of the '608 patent. "As a general proposition, when a trial court disposes finally of a case, any interlocutory rulings 'merge' with the final judgment. Thus both the order finally disposing of the case and the interlocutory orders are reviewable on appeal." *Hendler v. United States*, 952 F.2d 1364, 1368 (Fed.Cir.1991). The court turns first to the validity rulings.

*1070 A.

The court begins with Clontech's enablement arguments. The claims-in-suit describe genetically engineered RT without regard for the method used to mutate the genes. It is undisputed that by 1988 those skilled in the art knew several techniques for altering genetic sequences, including deletion and point mutations. The written description for the patents-in-suit describes how to implement the claimed invention by deletion mutation; the parties disagree as to whether it also teaches how to implement the claimed invention by point mutation. Clontech made at least one accused product, its PowerScript RT, by point mutation rather than deletion mutation.

[16] Enablement is a question of law, and the court reviews the judgment *de novo*. *See Koito Mfg. Co., Ltd. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1149 (Fed.Cir.2004); *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1194 (Fed.Cir.1999).

Clontech argues the district court erred, as a matter of law, in concluding that Invitrogen's claims are enabled. The contention rests on Invitrogen's failure to explain in the written description how to achieve RNase H minus RT with DNA polymerase using point mutation. Because the law requires the inventor to enable claims throughout their full scope without requiring undue experimentation by those having ordinary skill in the art, Clontech argues Invitrogen's written description fails to enable claims encompassing point-mutated RT.^{FN15} Recognizing that the

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claims-in-suit do not exclude point-mutated RT, Clontech concludes that the claims must be invalid for lack of enablement.

FN15. Invitrogen's arguments that the written description satisfies the enablement requirement, because it teaches point mutated RT, are without merit. Although the common written description explains that "a single amino acid change at a position 12 residues from the carboxy end of *E. coli* RNase H produces a 10-fold reduction in RNase H specific activity," "608 patent, col. 17, ll. 11-13, as explained infra with respect to the infringement judgment, the claims at issue are drawn to a complete absence of RNase H activity. Nothing in the record suggests that a "10-fold reduction" satisfies the "complete absence" limitation. This disclosure does not itself teach an enabling point mutation, nor does the record support a contention that the disclosure, coupled with the knowledge of those skilled in the art at in January 1987, enabled a point mutation.

[17][18] This argument mistakes the purpose of the enablement requirement. Section 112 requires that the patent specification enable "those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' " in order to extract meaningful disclosure of the invention and, by this disclosure, advance the technical arts.^{FN16} Koito Mfg., 381 F.3d at 1155 (quoting Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed.Cir.1997) (citation omitted)). Because such a disclosure simultaneously puts those skilled in the art on notice of the enforceable boundary of the commercial patent right, the law further makes the enabling disclosure operational as a limitation on claim validity. "The scope of [patent] claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope *1071 of what would be known to one of ordinary skill in the art without undue experimentation." Nat'l Recovery, 166 F.3d at 1196; see also In re Goodman, 11 F.3d 1046, 1050 (Fed.Cir.1993) ("[T]he specification must teach those of skill in the art 'how to make and how to use the invention as broadly as it is claimed'"); In re Fisher, 57 C.C.P.A. 1099, 427 F.2d 833, 839 (1970) ("[T]he scope of the claims must bear a rea-

sonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.").

FN16. The enablement requirement provides that "[t]he specification shall contain a written description ... of the manner and process of making and using [the invention] ... in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...." 35 U.S.C. § 112 (2000).

Although Clontech's validity argument might have force had Invitrogen limited its claims to modified RT by reference to point mutation, Clontech overlooks the fact that the claims are not limited by the method of achieving the mutation. As the district court noted, "[t]he enablement requirement is met if the description enables any mode of making and using the invention." Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1361 (Fed.Cir.1998); accord Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1335 (Fed.Cir.2003); Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533 (Fed.Cir.1991). In this case Invitrogen's teaching regarding deletion mutation is sufficient to satisfy its part of the patent bargain, as it fully teaches a mode of making the claimed invention.

Clontech mistakenly relies on our decision in National Recovery to support its nonenablement argument. In National Recovery the court affirmed judgment that a patent claim was invalid for lack of enablement. 166 F.3d at 1198. The claim was to a method, not a compound. The claimed method called for selecting certain signals for processing, yet the written description failed to teach one of ordinary skill in the art how to select among various candidate signals. Id. at 1196. A person of ordinary skill, reading the patent, would have been required to engage in undue experimentation before reaching a means of practicing the claimed method. In short, the National Recovery enablement problem concerned a failure to disclose any way to practice the claimed method. In this case, by contrast, Invitrogen fully described an operable method for achieving the claimed mutation.

[19] Enablement does not require the inventor to foresee every means of implementing an invention at

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pains of losing his patent franchise. Were it otherwise, claimed inventions would not include improved modes of practicing those inventions. Such narrow patent rights would rapidly become worthless as new modes of practicing the invention developed, and the inventor would lose the benefit of the patent bargain.

The court therefore affirms the district court's judgment that the claims at bar are not invalid for lack of an enabling disclosure on point mutation.

B.

1.

[20] The court turns to Clontech's written description argument.^{FN17} The three patents-in-suit each claim a genetically modified RT in terms of its RNase H and DNA polymerase behavior. Claim 1 of the '608 patent is representative. It provides

FN17. Section 112 requires that "[t]he specification shall contain a written description of the invention...." 35 U.S.C. § 112, ¶ 1 (2000) (emphasis added). This "written description" requirement is distinct from the enablement requirement, as discussed in the previous section. *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 920 (Fed.Cir.2004); *Enzo Biochem Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 963 (Fed.Cir.2002).

*1072 1. An isolated polypeptide *having DNA polymerase activity* and substantially reduced RNase H activity, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in said polypeptide *having substantially reduced RNase H activity*, and wherein said nucleotide sequence is derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents. '608 patent, col. 19, lines 26-34 (claim 1) (emphases added). With these patents Invitrogen thereby claims a compound (the polypeptide or genetically engineered RT) in terms of biological functions (DNA polymerase and RNase H activity).

Clontech filed for summary judgment, arguing that

this fashion of claiming the modified RT fails the § 112 written description requirement and renders the claims-in-suit invalid.^{FN18} Invitrogen opposed and filed a cross-motion that the claims were not invalid on this ground.

FN18. Claims 3 and 4 of the '797 patent do not follow the compound-by-biologic-function model exemplified in the '608 patent, claim 1. Clontech excluded these two claims from this written description challenge.

The district court tested the common written description of the patents-in-suit against the PTO guidelines. The guidelines state that the written description requirement of 35 U.S.C. § 112, ¶ 1, can be met by

show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, "Written Description" Requirement, 66 Fed.Reg. 1099, 1106 (Jan. 5, 2001).^{FN19} The court adopted this standard in *Enzo Biochem Inc. v. Gen-Probe, Inc.*, 323 F.3d at 964.

FN19. In *University of Rochester* the court reaffirmed its approval of *Enzo*'s use of the PTO written description guidelines. 358 F.3d at 925.

The district court ruled that (1) the common written description, (2) testimony from Invitrogen's expert, Dr. Champoux, and (3) an article by Johnson et al., 83 *Proc. Nat'l Acad. Sci. USA* 7648-52, 7651 (1986), established a sufficiently known correlation between RNase H activity in RT (function) and the RT gene made by deletion mutation (structure) to satisfy the PTO test for written description. The court concluded that the undisputed evidence was entirely one sided in favor of Invitrogen, and granted partial summary judgment, ruling that the claims at issue were not invalid for lack of written description.

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2.

[21][22] Unlike conception and enablement, compliance with the written description requirement is a question of fact. Enzo Biochem, 323 F.3d at 962-63; Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed.Cir.1991). Like the facts underlying conception and enablement, invalidating a claim requires a showing by clear and convincing evidence that the written description requirement has not been satisfied. Enzo Biochem, 323 F.3d at 962. In response to Invitrogen's partial summary judgment motion, the law required Clontech to come forward with evidence raising at least a genuine issue of fact *1073 regarding whether the patents failed the written description requirement. Novartis Corp. v. Ben Venue Labs., Inc., 271 F.3d 1043, 1046 (Fed.Cir.2001).

3.

Clontech argues that University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed.Cir.1997) compels the conclusion that the claims-in-suit fail the written description requirement. In Eli Lilly, this court found a claim to mammalian DNA for insulin unsupported by a written description reciting only the nucleotide sequence of rat cDNA for insulin. *Id.* at 1567-68. Clontech maintains that it was error not to determine, as a matter of law, that all but two claims in the patents-in-suit fail the written description requirement of § 112, ¶ 1 because they “do not recite the DNA or protein sequences as required” by Eli Lilly, *id.* at 1566-69, and Fiers v. Revel, 984 F.2d 1164, 1171 (Fed.Cir.1993). Thus, according to Clontech, the district court erred in finding sufficient structure in the DNA sequence recited in the common specification, and within the knowledge of one of ordinary skill in the art, because the claims at issue “are not limited to sequences recited in the specification and do not recite DNA or protein sequences.”

This argument is misplaced. First, the district court found it undisputed that in addition to the sequence recited in the specification at bar, “at the time of the invention, the sequences of RT genes were known and members of the RT gene family shared significant homologies from one species of RT to another.” The written description teaches that the invention can be applied to RT genes of other retroviruses including HTLV-1, BLV, RSV, and HIV. *See, e.g.*, 608

patent, col. 9, ll. 34-54. As Invitrogen's expert explained, the specification cites references providing the known nucleotide sequences of these RT genes. *Id.*, col. 9, ll. 47-54; January 24, 2002 Champoux Decl. ¶ 4. Finally, Champoux's declaration established that the sequences for these and other representative RT genes were known in the art by January 1988. *Id.* ¶¶ 4-7. Clontech has not adduced contrary evidence establishing a genuine issue of fact, and we discern no error in the district court's analysis. Clontech's written description challenge, in short, proceeds from a factual premise contrary to the record.

Second, Clontech's appeal to Eli Lilly and Fiers is misplaced. In those cases, the patent specifications at issue did not identify the sequence (structure) of any embodiment of DNA claimed therein. *See Eli Lilly*, 119 F.3d at 1567-68 (affirming a judgment that the claim requiring cDNA encoding human insulin was invalid for failing to provide an adequate written description where the specification described the human insulin A and B chain amino acid sequences encoded by the cDNA, but did not provide the nucleotide sequence for the cDNA itself); Fiers, 984 F.2d at 1167-68, 1170-71 (finding the written description insufficient where the patent claimed purified DNA encoding human fibroblast interferon-beta polypeptide, but the specification only disclosed a bare reference to DNA and suggested a process to sequence it). In contrast, the shared written description for the patents-in-issue recites both the DNA and amino acid sequences of a representative embodiment of the claimed RT enzyme. The specification also discloses test data that the enzyme produced by the listed sequence has the claimed features-DNA polymerase activity without RNase H activity. Under both the Eli Lilly and Fiers analysis, the specification at bar is sufficient.

In short, there is no error in the district court's ruling that the claims in the patents-in-suit*1074 satisfy the written description requirement of § 112.

* * * * *

In sum, the district court erred in granting judgment of invalidity under § 102(g)(2). Clontech's challenges to the court's partial summary judgments on written description and enablement are misplaced and fail to support the invalidity judgment. Accordingly, the court vacates the judgment of invalidity and the conception ruling on partial summary judgment, and

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remands for further proceedings.

[23] On remand, we remind the district court that the material factual dispute we perceive regarding appreciation affects not only the proper date of conception, but also the date of reduction to practice. “It is now well settled that in [an accidental creation] there is no conception or reduction to practice where there has been no recognition or appreciation of the existence of the new form.” *Silvestri*, 496 F.2d at 597. Because we reserve the question of appreciation for the jury, its determination on this issue will decide the date of conception (as well as reduction to practice).

IV.

[24] Finally, Clontech cross-appeals the district court's partial summary judgment that the PowerScript RT infringes claims 3, 4, 12, and 13 of the '608 patent.'

A.

Each claim at issue depends from claim 1 of the '608 patent'. As noted in the preceding discussion, independent claim 1 provides:

1. An isolated polypeptide having DNA polymerase activity and *substantially reduced RNase H activity*, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in said polypeptide having *substantially reduced RNase H activity*, and wherein said nucleotide sequence is derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents.

'608 patent', col. 19, ll. 26-34 (claim 1) (emphases added).

In 2001, the trial court determined that 178 claims in the '608 patent', reciting the limitation “substantially reduced RNase H activity,” were invalid as indefinite under § 112. See *Invitrogen*, slip op. (D.Md. May 4, 2001) (opinion and order granting partial summary judgment of invalidity) (“May 4 PSJ Order”); *Invitrogen Corp. v. Clontech Labs., Inc.*, slip op. (D.Md. Aug. 8, 2001) (R & R recommending clarifications to May 4 PSJ Order); *Invitrogen Corp. v. Clontech*

Labs., Inc., slip op. (D.Md. Oct. 4, 2001) (order adopting the Aug. 8, 2001 R & R on validity). Although the district court invalidated independent claim 1, eighteen other claims in the '608 patent'—including dependent claims 3, 4, 12, and 13—survived Clontech's challenge.

Dependent claims 3 and 4 provide:

3. The polypeptide of claim 1, wherein said polypeptide *has no detectable RNase H activity*.
4. The polypeptide of claim 1, wherein said polypeptide *lacks RNase H activity*.

'608 patent', col. 19, ll. 38-41 (emphases added). In the May 4 PSJ Order, the court ruled that “no detectable RNase H activity” and “lacks RNase H activity” had “sufficient clarity to alert those of ordinary skill in the art of the metes and bounds of the invention,” and thus were not invalid for indefiniteness. See May 4 PSJ Order at 16.

Claims 12 and 13 further provide:

- *1075 12. The polypeptide of claim 1, wherein said polypeptide allows an mRNA template to remain intact during cDNA synthesis as shown in FIG. 5.
13. The polypeptide of claim 1, wherein said polypeptide allows an mRNA template to remain intact during a one minute cDNA synthesis reaction as shown in FIG. 5.

'608 patent', col. 19, ll. 62-67. Figure 5 of the '608 patent', as recited in claims 12 and 13, reprints a photograph of a gel assay. The specification describes that gel assay as confirming that a plasmid with the claimed, modified RT gene, encoded RT that “completely lacked RNase H activity.” '608 patent', Fig. 5 & col. 16, ll. 33-49.

The limitation “substantially reduced RNase H activity” in claim 1 of the '608 patent' resembles the limitation “substantially no RNase H activity” in independent claim 1 of the earlier '005 patent'. That claim reads in full:

1. An isolated DNA molecule comprising a nucleotide sequence encoding a polypeptide having DNA

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polymerase activity and *substantially no RNase H activity*, wherein said nucleotide sequence is derived from a Moloney murine *leukemia* virus (M-MLV) nucleotide sequence.

'005 patent, col. 19, ll. 2-6 (claim 1) (emphasis added). The same "substantially no RNase H activity" limitation appears in the '797 patent claims. See, e.g., '797 patent, col. 19, ll. 17-25 (claim 1).

After the district court adjudged the '797 and '005 patents unenforceable in 1999, Clontech set about developing a competing product. In a July 18, 1999 laboratory notebook entry, Clontech's scientist Dr. Steven Hendricks wrote he would "now focus on generating an RNase H minus form of the MMLV RT." The entry identified "D524N" as one "potential mutant already cloned" and predicted that the changes to it "should completely inactivate the RNase H activity."

Testing the D524N-encoded RT by the solubilization assay described in the patents-in-suit, on August 3, 1999, Hendricks wrote in his laboratory notebook, "NO SIGNIFICANT RNase H activity detected in the preparation of the D524N mutant!!!" The D524N mutant RT became the basis of Clontech's PowerScript RT. Numerous Clontech internal documents and marketing materials, including their website, further touted the PowerScript RT as "lacking" in or that it "eliminates" RNase H activity.

Invitrogen sought partial summary judgment that Clontech's PowerScript RT infringed claims 3, 4, 12, and 13 of the '608 patent. On February 21, 2003, the Special Master recommended granting Invitrogen's motion in part and finding literal infringement. *Invitrogen*, (D.Md. Feb. 21, 2003) (R & R regarding Invitrogen's infringement motion) ("Infringement R & R"). On April 21, 2003, after reviewing the record *de novo*, the district court adopted the recommendation over Clontech's objection and granted partial summary judgment of literal infringement on all four claims. Clontech appeals.

B.

[25][26][27][28] This court reviews *de novo* the district court's partial summary judgment of infringement. See *SanDisk Corp. v. Memorex Products, Inc.*, 415 F.3d 1278, 1283 (Fed.Cir.2005); *Hilgraeve Corp.*

v. McAfee Assocs., Inc., 224 F.3d 1349, 1352 (Fed.Cir.2000). The trial court's claim construction is a legal issue that we review *de novo*. See *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454 (Fed.Cir.1998) (en banc). The court's comparison of the properly construed claims to the accused products is a factual matter, **1076Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1323 (Fed.Cir.2002), and in reviewing the trial court's partial summary judgment this court ascertains, as a matter of law, whether the trial court overlooked genuine issues of fact weighing against infringement.

A material factual dispute must be genuine. "[T]he mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment." *Anderson*, 477 U.S. at 247-48, 106 S.Ct. 2505. A genuine dispute requires evidence "such that a reasonable jury could return a verdict for the non-moving party." *Id.* at 248, 106 S.Ct. 2505. Evidence that is "merely colorable," or is "not significantly probative," will not prevent summary judgment. *Id.* at 249-50, 106 S.Ct. 2505. Of course, in assessing a putative dispute "the judge's function is not himself to weigh the evidence and determine the truth of the matter but to determine whether there is a genuine issue for trial." *Id.* at 249, 106 S.Ct. 2505.

C.

Clontech challenges the district court's claim construction, defining claims 3, 4, 12, and 13 by reference to gel assay results. Instead, Clontech argues, under a proper construction each claim must be limited to the results of a solubilization assay. We disagree.

[29] Claim construction requires the court to determine the meaning of disputed claim terms to one of ordinary skill in the art at the time of the invention. See 35 U.S.C. § 112; *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed.Cir.2005) (en banc); *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1360 (Fed.Cir.2004); *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1332 (Fed.Cir.2001). The court determines this meaning by examining the claim language, as it relates to the invention set forth in the written description, the drawings, and where relevant the prosecution history. See *Phillips*, 415 F.3d at 1313-17; *Vitronics Corp. v. Con-*

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ceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996).

1.

The court necessarily begins with the language of the asserted claims. See Phillips, 415 F.3d at 1312; Bell Commc'ns Research, Inc. v. Vitalink Commc'ns Corp., 55 F.3d 615, 619-20 (Fed.Cir.1995). Clontech does not challenge the trial court's conclusion that "no detectable RNase H activity" and "lacks RNase H activity" mean "a complete absence of RNase H activity" to one of skill in the art. Although Invitrogen suggests, *inter alia*, that "no detectable" and "lacks" might have different meanings, Invitrogen does not provide any cogent argument explaining why there is error in this trial court ruling. Thus, notwithstanding the presumption that "no detectable" in claim 3 and "lacks" in claim 4 have different scopes, see Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed.Cir.1998), we take the parties as conceding claims 3 and 4 both mean "a complete absence of RNase H activity."

Focusing on the terms "no detectable" and "lacks," neither can be understood without reference to the written description because each limitation begs the question of how one of skill in the art would understand the patent specification as describing how to measure RNase H activity for claims 3 and 4. See Phillips, 415 F.3d 1303, 1312. Although the '608 patent specification does not expressly define either term, it unmistakably teaches how one skilled in the art would determine that a mutant RT "completely lacks" RNase H activity. See '608 patent, col. 16, ll. 33-49.

*1077 The specification explains that "[t]o confirm" that a claimed mutant RT "completely lacked" RNase H activity, the inventors undertook a specific gel assay. The specification describes the assay in detail, and provides the results in Fig. 5. *Id.*, ll. 33-45. Fig. 5 compares the RNase H activity of the mutant RT (Fig.5A) to unaltered MMLV RT (Fig.5B).^{FN20} The written description further notes that, "[i]n addition," the same mutant RT showed no RNase H activity under a solubilization assay. *Id.*, col. 16, ll. 45-49. With this primacy placed on the gel assay results, the patent unmistakably instructs one skilled in the art to measure RNase H activity, for purposes of claims 3 and 4, by using a gel assay. This establishes the gel assay as being both necessary and sufficient to meas-

ure RNase H activity for claims 3 and 4.

^{FN20} See '608 patent, col. 12, ll. 50-60 (describing pRT601 as encoding MMLV RT); *id.*, col. 15, l. 29-col. 16, l. 32 (describing creation of deletion plasmid pRTdEcoRV-C from pRT601); *id.*, col. 16, ll. 33-45 (explaining comparison, shown in Fig. 5, of RNase H activity from mutated RT and wild RT).

Although the written description might teach a different mix of gel assay and solubilization results as sufficient to show different levels of RNase H activity, as explained above the parties concede that the claims speak only to a "complete absence" of such activity. This points the court directly to the passage discussed above, and establishes the gel assay as determinative of the claimed behavior.

For the same reasons, the specification even more strongly indicates that the gel assay is the proper means for determining compliance with claims 12 and 13, each of which expressly references Fig. 5 in the patent and points the person of skill in the art to this discussion in the specification.^{FN21} Clontech's contrary reading simply cannot be squared with either the plain language of claims 12 or 13, or the relevant portions of the '608 patent specification.

^{FN21} In its opening brief to this court, Clontech did not set forth a separate argument for reading claims 12 or 13 to require a solubilization assay, to the exclusion of a gel assay. Instead, Clontech lumps claims 12 and 13 into the argument discussed above with regard to claims 3 and 4. In its reply, Clontech raises a new argument in support of its contention that a gel assay was foreclosed by the stipulated definition of "substantially no RNase H activity."

This reply argument renews Clontech's earlier argument to the Special Master, with specific reference to claims 12 and 13. Invitrogen did not seek permission to file a supplemental brief responding to this new contention, and the issue was not reached at oral argument. Nevertheless, we view this belated argument by Clontech as improper and do not consider it.

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See Novosteel SA v. United States, 284 F.3d 1261, 1274 (Fed.Cir.2002) (litigant waives argument not presented in opening brief). Clontech waived this argument by failing to raise it in its opening brief on the cross-appeal.

Clontech's arguments to the contrary are without merit. Clontech attempts to link the meaning of "no detectable" and "lacks" to the stipulated definition of "substantially no RNase H activity".^{FN22} Clontech*1078 argues that these terms must mean less RNase H activity than the amount satisfying the stipulated definition of "substantially no RNase H activity" in the '797 and '005 patents. We disagree.

^{FN22}. On June 22, 1999, the district court signed a stipulated order, defining an RT with "substantially no RNase H activity" as

a reverse transcriptase purified to near homogeneity and having an RNase H activity of less than 0.001 pmoles [³H](A)_n solubilized in 20 minutes per g protein in a reaction volume of 50 μ l wherein the [³H](A)_n is solubilized from a [³H](A)_n • (dT)_n substrate in which the [³H](A)_n has a specific radioactivity of 2,200 cpm/pmole.

Life Techs., Inc. v. Clontech Labs., Inc., slip op., No. AW-96-4080 (D.Md. June 22, 1999) (stipulation and order). The parties agree that by its terms, testing RT RNase H activity against this stipulated definition requires using a solubilization assay.

This stipulated definition corresponds, not surprisingly, verbatim to the definition of "substantially no RNase H activity" in the common written description of the patents-in-suit. *See, e.g., '608 patent*, col. 9, ll. 21-26.

[30] First, Clontech points to the '608 patent prosecution history. The court examines the prosecution history, when pointed out and placed in evidence, to ascertain if a proffered claim construction has been disclaimed. *See* 415 F.3d 1303, 1317, 415 F.3d 1278, 1286-87; *Medrad, Inc. v. MRI Devices Corp.*, 401

F.3d 1313, 1319 (Fed.Cir.2005) ("We cannot look at the ordinary meaning of the term ... in a vacuum. Rather, we must look at the ordinary meaning in the context of the written description and the prosecution history."); *Vitronics*, 90 F.3d at 1582. Clontech argues that claim 1 of the '608 patent (and thus the dependent claims 3 and 4), as originally filed, required "substantially no" instead of "substantially reduced" RNase H activity. But as Clontech further notes, Invitrogen cancelled those originally-filed claims and added new claims drawn to the "substantially reduced RNase H activity" limitation in the issued claim 1. Indeed, as Invitrogen observes, it cancelled those original limitations by preliminary amendment with its continuation application, meaning the "substantially no RNase H activity" limitation was never presented to the PTO for examination as part of the '608 patent. Nonetheless, because Invitrogen sought, in the prosecution, to distinguish prior art having "reduced" RNase H activity, Clontech concludes "substantially reduced" must mean less RNase H activity than the failed "substantially no" limitation in the original claim.

[31] To the extent that this represents a prosecution disclaimer or prosecution history estoppel argument, it falters on the principle that the prosecution of one claim term in a parent application will generally not limit different claim language in a continuation application. *See ResONet.com, Inc. v. Lansa, Inc.*, 346 F.3d 1374, 1383 (Fed.Cir.2003); *Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308, 1322 (Fed.Cir.1999); *cf. Biogen, Inc. v. Berlex Labs., Inc.*, 318 F.3d 1132, 1141 (Fed.Cir.2003) ("When an applicant is seeking different claims in a divisional application, estoppel generally does not arise from the prosecution of the parent."). Although the court recognizes an exception where an amendment to a related limitation in the parent application distinguishes prior art and thereby specifically disclaims a later (though differently worded) limitation in the continuation application, *see, e.g., Elkay Mfg. Co. v. EBCO Mfg. Co.*, 192 F.3d 973, 978-79 (Fed.Cir.1999), Clontech nowhere explains how that exception would apply in this case. Nor does Clontech explain how any prior art distinguished in the '797, '005, or '608 patent prosecutions operates to disclaim use of a gel assay to show "complete absence" of RNase H activity in claims 3 and 4 of the '608 patent. The prosecution history presented to the court does not impose such a limitation. The fact that the parties stipulated to a definition of "substantially no RNase H activity," drawn verbatim from

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the wording of an express definition in the written description, does not mandate that the different limitations at issue here be given the same construction. To the contrary, the use of the distinct terms “substantially reduced” and “no detectable” and “lacks” canonically suggests that these limitations be given a different scope than the limitation to which the parties stipulated. See *Comark*, 156 F.3d at 1187.

Second, Clontech argues that the district court's “complete absence” definition, by its plain meaning, requires construing *1079 claims 3 and 4 consistent with the stipulated definition of “substantially no RNase H activity” in the '797 and '005 patents. Nothing in the notion of “complete absence of RNase H activity” in the '608 patent requires consideration in view of the “substantially no RNase H activity” limitation set forth in the '797 and '005 patents and defined by the stipulated order. Nor is it proper to read provisions in the '608 patent written description, pertaining to the “substantially no RNase H activity” limitation in the parent applications, into the meaning of claims 3 and 4 in the '608 patent. See *id.*, 156 F.3d at 1186-87 (discussing the prohibition against reading limitations from the specification into the claims). These are not, as Clontech presupposes, isolated terms with abstract meanings amenable to easy comparison such as by referencing a thesaurus; rather, these are claim terms with defined meanings rooted in the particular context of different patents and patent claims.

Thus, the court finds no error in the district court's analysis, under which the complete absence of RNase H activity for claims 3, 4, 12, and 13 must be shown by the gel assay as set forth in the written description of the '608 patent.

D.

[32] Finally, Clontech contends the district court erred in failing to credit factual disputes precluding partial summary judgment of literal infringement. First, it argues that the district court ignored the disagreement between Dr. Falkinham, its expert, and Dr. Champoux, Invitrogen's expert, regarding how to interpret gel assays measuring the PowerScript RT RNase H activity. Second, Clontech maintains that gel assay results from 1993, in an article by Blain and Goff regarding the D524N mutant RT, proved that the RT had measurable RNase H activity and thus

could not infringe the claims at issue.^{FN23} We disagree.

^{FN23} Stacy W. Blain & Stephen P. Goff, *Nuclease Activities of Moloney Murine Leukemia Virus Reverse Transcriptase: Mutants with Altered Substrate Specificities*, 268 J. Biological Chemistry 23585 (1993) (“Blain & Goff 1993”). In that article Blain and Goff explain D524N comprises a point mutation to the wild-type MMLV RT gene. *Id.* at 23586-87. The article concludes that the D524N mutant RT had between 10 and 25% the RNase H activity of wild-type MMLV RT.

Although Falkinham and Champoux disagreed regarding how to interpret Invitrogen's gel assay evidence, measuring the PowerScript RT RNase H activity, the district court correctly determined that Falkinham's disagreement did not create a genuine dispute for infringement. Champoux explained that a gel assay works by separating molecules according to their size. Similarly sized fragments move to the same location on the gel. The RT, by its RNase H activity, cuts mRNA into fragments. As Champoux explained, the resulting fragments should have a random size distribution, because the RT cuts the mRNA at random points. This appears on a gel assay as a visual “smear,” since the differently sized fragments will sort to different positions in the gel assay lane. But without RNase H activity, the mRNA will remain intact. All similarly sized mRNA molecules migrate to the same location in the gel assay, manifested visually as a band at a particular location. The district court found this explanation consistent with both the '608 patent specification, as it discusses gel assay,^{FN24} and the usage in a *1080 1996 article by Blain and Goff.^{FN25}

^{FN24} The '608 patent specifically calls for using a gel assay to assess “the effect of cDNA synthesis upon the integrity of the template RNA.” ‘608 patent, col. 14, ll. 6-7. It describes Fig. 5-a gel assay result-as demonstrating pRT601 (a wild-type MMLV RT) “totally degraded” a 2.3 kilobase mRNA template after five minutes of synthesis. ‘608 patent, col. 16, ll. 36-38. As Champoux explained, Fig. 5b shows a “smear” or distribution of fragment sizes in the five minute lane

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of the gel assay. By comparison, gel assay confirming the claimed mutant RT “completely lack [ed]” RNase H activity shows a clear band at 2.3 kilobases. *See* ‘608 patent, Fig. 5a & col. 16, ll. 33-40.

FN25. Stacy W. Blain & Stephen P. Goff, *Differential Effects of Moloney Murine Leukemia Virus Reverse Transcriptase Mutations on RNase H Activity in Mg²⁺ and Mn²⁺*, 271 J. Biological Chemistry 1448 (1996) (“Blain & Goff 1996”).

Neither side disputed that Blain and Goff were persons of ordinary skill in the art. In the 1996 article, Blain and Goff used gel assays to measure the RNase H activity of various RT samples. Consistent with Champoux's explanation, Blain and Goff relied on the proposition that identically sized fragments should migrate to the same position, and form a band, in a gel assay lane. *See* Blain & Goff 1996, *supra* at 1449-51. Moreover, discussing a “smear” in one gel assay, *id.* at 1450, fig. 2, lane 7, they explained it “presumably corresponded to a heterogenous population of DNA with various sized RNA species still annealed.” *Id.* at 1451. E.g., a “smear” indicates—as Champoux explained—a mixture of differently sized molecular fragments.

Falkinham offered a very different view of how gel assay works. He opined that Invitrogen's gel assay experiments must be understood by evaluating the area of the bands representing the mRNA fragments left after exposure to the PowerScript RT. Claiming that Invitrogen's test results showed the ‘band area’ to be decreasing with incubation time, Falkinham concluded that this could only be explained by the presence of RNase H activity. He explained that the fragments produced by such activity could not be seen because they would have “small size.” Nowhere did Falkinham explain why the PowerScript RT would only create small sized fragments with its RNase H activity, nor reference any theory explaining-or evidence confirming-this behavior.

[33] The district court correctly concluded that “Dr. Falkinham's assertions do not rise to the level of

genuine issues of fact[.]” Infringement R & R at 6. Given that there is no dispute that Blain and Goff were persons of ordinary skill in the art, and given the accord between Blain and Goff, the ‘608 patent, and Champoux on how to read a gel assay, no reasonable juror could find for Clontech based on Falkinham's speculative difference of opinion. **FN26** A party does not manufacture more than a merely colorable dispute simply by submitting an expert declaration asserting that something is black when the moving party's expert says it is white; there must be some foundation or basis for the opinion. *See Anderson*, 477 U.S. at 247-48, 106 S.Ct. 2505 (“[T]he mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment.”). Had Falkinham cited some basis for his opinion that the RNase H would yield “small sized” mRNA fragments, Clontech may have identified a genuine issue. But he did not, and this portion of his declaration does not prevent partial summary judgment. *See Anderson*, 477 U.S. at 249-50, 106 S.Ct. 2505 (holding *1081 that insufficiently probative evidence will not prevent summary judgment).

FN26. Clontech argues that the district court made improper credibility determinations in concluding Falkinham failed to raise a genuine issue, compelling vacatur. Although the Special Master did write “the credible evidence overwhelmingly supports Dr. Champoux,” *Invitrogen R & R* at 8, we do not read the court's opinion as relying on a credibility determination. Elsewhere, the Master specifically explained Falkinham's assertions failed to create a genuine issue; and, moreover, the Master follows the “credible evidence” statement with detailed discussion of the competing evidence.

The district court also correctly determined that Blain and Goff's 1993 results did not create a genuine issue. Although the 1993 paper reported some measurable RNase H activity in the D524N mutant RT, from which Clontech derived its PowerScript RT, the 1996 paper reveals error in that 1993 measurement. The 1993 article described results from a gel assay that was comparable to neither the one described in the patent, as conducted by Champoux, nor the one discussed in the 1996 article by Blain and Goff. In the 1996 article they explained why their 1993 result was

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anomalous and showed that the D524N mutant had no RNase H activity. The 1996 paper was motivated by, and directed at, explaining why the 1993 test results were wrong. Nonetheless, Clontech argues that “if anything is to be drawn from the 1996 Blain and Goff article, it is the finding that PowerScript (D524N) has measured RNase H activity ... and thus cannot infringe as a matter of law.” We disagree.

As Invitrogen observes, the 1996 article reports that—when problems with the gel assay substrate from 1993 are corrected, and using gels corresponding to those described in the '608 patent specification and used in Invitrogen's assay—D524N showed no RNase H activity. Noting this fact, and noting the 1993 gel assay did not correlate to the gel assay described in the '608 patent, the district court correctly determined that the 1993 results were not relevant to the infringement analysis. Infringement R & R at 12. Thus, nothing in these articles creates a genuine dispute that would prevent partial summary judgment of infringement.

Because Clontech shows no error in the partial summary judgment that its PowerScript RT literally infringes claims 3, 4, 12, and 13 of the '608 patent, we affirm.

V.

We hold as follows. First, we vacate the judgment of invalidity and the district court's partial summary judgment on Goff's conception. Second, we affirm the partial summary judgments that the claims-in-suit are enabled, and that they satisfy the written description requirement of § 112. Finally, we affirm the partial summary judgment that Clontech's PowerScript RT literally infringes claims 3, 4, 12, and 13 of the '608 patent. We remand for further proceedings consistent with this opinion.

AFFIRMED-IN-PART, VACATED-IN-PART, RE-MANDED.

COSTS

No costs.

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